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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ST98008	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/FR99/00643	International filing date (*day/month/year*) 19 March 1999 (19.03.99)	Priority date (*day/month/year*) 24 March 1998 (24.03.98)
International Patent Classification (IPC) or national classification and IPC C12N 15/87		
Applicant AVENTIS PHARMA S.A.		

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1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28 September 1999 (28.09.99)	05 July 2000 (05.07.2000)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR99/00643

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☐ the international application as originally filed.

☐ the description, pages 1-38, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, Nos. 1-42, as originally filed,
Nos. _____, as amended under Article 19.
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,
Nos. _____, filed with the letter of _____.

☒ the drawings, sheets/fig 1/13-13/13, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/FR99/00643

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 39-40

because:

☒ the said international application, or the said claims Nos. 3-40 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See Supplemental Box

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____ .

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.

This Authority considers that the subject matter of Claims 39-40 is subject to the provisions of PCT Rule 67.1(iv). No opinion will therefore be given concerning the industrial applicability of the subjects of these claims (PCT Article 34(4)(a)(i)).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-42	**YES**
	Claims		**NO**
Inventive step (IS)	Claims	1-42	**YES**
	Claims		**NO**
Industrial applicability (IA)	Claims	1-38, 41-42	**YES**
	Claims	39-40 (see Box III)	**NO**

2. Citations and explanations

The invention relates to new vectors including a double-stranded DNA molecule and an oligonucleotide covalently coupled to a targeting signal peptide sequence, the latter being capable of forming a triple helix with a sequence specific to the double-stranded DNA. Such a construction enables the use of the vectors for transferring nucleic acids into specific cells or cell compartments.

Document D1, which is considered to be the closest prior art, describes the covalent coupling of double-stranded DNA to an NLS-type targeting peptide sequence but does not mention a sequence capable of forming a DNA triple helix.

Document D2 does mention the formation of oligonucleotide triple helices but in the absence of coupling to a targeting sequence. In D2, the oligonucleotide is coupled with a photoactivatable alkylating agent such as psoralen in order to study recombination phenomena *in vivo*. Consequently, the invention is considered to be novel and inventive (PCT Article 33(2) and 33(3)).

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Claim 1 mentions coupling an oligonucleotide to a "targeting signal". Such a designation is clearly open to interpretation as it does not define the type of coupling (covalent bond, electrostatic interaction, etc.) and does not give any definition of the type of signal (it may be of any kind, without specifying the nature of the target, etc.) owing to the absence of technical content enabling the scope of protection to be delimited. Thus on pages 13-14 of the description, the applicants speak of these signals having a "varied" nature by mentioning peptide, glucide or hormone signals.

2. In all of Examples 1-10, only the NLS targeting signals enable demonstration of the feasibility of the invention and of the fact that the desired technical effect has been achieved (targeting and vector expression in the nucleus). It is for this reason that, except for these peptide NLS signals, the coupling of oligonucleotides to other types of targeting signals, as well as the functionality thereof *in vitro* or *in vivo*, are not supported by the description.
   Moreover, in certain specific cases, a person skilled in the art could be prompted to seek new chemical coupling methods in order to test the effectiveness of the targeting of the resulting vector, while taking care to prevent such "localisation" from interfering with the expression of said vector.

VIII. Certain observations on the international application

As a result, Claim 1 does not comply with PCT Articles 5 and 6.